REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

Claims 1-10, 22, 26, 40, 42-44, 46, 50, 53, 54, 56, 58, and 63-108 are pending in the application. Claims 1-10, 12, 40, 43, 44, 46, 50, 70-84, 98, 99, 104, and 105 are withdrawn from consideration. Claims 22, 26, 42, 53, 54, 56, 58, 63-69, 85-97, 100-103 and 106-108 are under consideration and stand rejected.

No amendment has been made to the clams.

Rejection under 35 U.S.C. § 112

A single rejection has been maintained in this application. Claims 22, 26, 42, 53, 54, 56, 58, 63-69, 85-97, 100-103 and 106-108 remain rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. The rejection is respectfully traversed for at least the following reasons, which are proven by the evidence submitted herewith pursuant to 37 C.F.R. § 1.132, in addition to the reasons that have been previously stated, which are likewise borne-out by the evidence submitted herewith.

In stating and maintaining the rejection, the Office has alleged that the specification, claims and the art do not adequately describe the distinguishing features or attributes shared by the members of the claimed genus comprising DNA constructs for gene silencing comprising the recited sense and antisense nucleotide sequences and further comprising an intron sequence, whereby any intronic sequence is inserted anywhere in the chimeric DNA, and whereby the DNA construct provides for the function claimed, of generating a gene silencing construct that reduces the phenotypic expression of a nucleic of interest in any

plant cell and in any isolated eukaryotic cell. *See, e.g.,* OFFICE ACTION MAILED FEBRUARY 8, 2006, at 4, lines 3-9. In the reasons alleged by Office for maintaining the rejection, the Office has specifically challenged the sufficiency of the description in the specification of "any intronic sequence, inserted anywhere in the chimeric DNA."

The Office acknowledges that the specification teaches fully complementary pair constructs for reducing the phenotypic expression of a transgenic GUS gene and for reducing the phenotypic expression of the Δ12 desaturase target gene in Arabidopsis which complementary pair constructs additionally comprise the pyruvate orthophosphate dikinase 2 intron from Flaveria trinervia in forward or reverse orientation. OFFICE ACTION MAILED FEBRUARY 8, 2006, at 4, lines 10-22. However, the Office alleges that the specification nevertheless fails to teach or adequately describe a representative number of species in the genus such that the common attributes or characteristics concisely identifying members of the proposed genes are exemplified. *Id.*

In rebuttal to the alleged reasons for the rejection stated in the Office Action mailed June 6, 2006 which was also directed in part to "the presence of any intron anywhere in the chimeric DNA," Applicants provided several post-application publications including Smith et al., *Nature*, 407:319-20, 2000, which is where results disclosed in the present application were published in a peer reviewed journal, Wesley et al., *The Plant Journal*, 27:581-90, 2001, and a selection of additional publications reporting on the use of chimeric genes encoding double stranded RNA and comprising an intron that referenced Smith et al., 2000.

The Examiner responded to Applicants' arguments and evidence in the Office Action mailed February 8, 2007 at pages 5-8. In response to those remarks, Applicants note that the Examiner did not specifically address Wesley et al. 2001, which was provided to support the objective truth of the teaching in the specification that the location of the intron is not critical.

In regard to Smith et al. the Examiner indicated that the additional examples described in Smith et al. do not provide adequate description for the broad genus claimed. However, Applicants point out that Smith et al. was not provided for this purpose.

Smith et al. demonstrated that the teaching of the current specification to include an intron in a dsRNA encoding a chimeric gene silencing construct for the purpose of enhancing the efficiency of silencing a target gene of interest, which was disclosed in the present application and reiterated in the peer reviewed publication by Smith et al., 2000, has been quickly adopted by the scientific community. The frequent reference to Smith et. al., 2000, in the subsequent scientific literature proves that the results presented by the authoring scientists was not considered to limit the use of intron sequences to the particular intron exemplified in the current application. Rather, those of ordinary skill in the art upon learning of the results disclosed in the present application and published in Smith et al., 2000, readily and widely adopted the teachings to make and use a genus of constructs broadly consistent with what is presently claimed. The teachings of the present application in Smith et al. conveyed a broad genus of constructs to practitioners in the art, which is clearly demonstrated by the numerous citations to Smith et al. by various practitioners. Because it is more common to cite peer reviewed publications rather than patent applications, Smith et al., 2000, was provided to show the connection between the teachings in the present application that were published in Smith et al. 2000, and how those teachings were adopted in the art.

Smith et al., 2000, and the wide adoption of its teachings as a general tool in the sciences proves that persons of ordinary skill in the art would have, indeed did, appreciate the general applicability of teachings in the present application that describe the claimed subject matter. This proves that persons of ordinary skill in the art would have recognized that the teachings of the present application demonstrated that the present inventors were in

"possession" of the general invention of the gene silencing constructs prepared according to the principals described in the specification and recited in the present claims.

The Examiner also referred to questions posed by Smith et al. allegedly regarding the ability to enhance gene silencing by inserting intron sequences. Applicants respectfully submit that these "questions" do not concern the ability to enhance gene silencing, rather amount the mechanistic process of the enhancement. Such questions do not concern the sufficiency of a disclosure as it is well established that an inventor need not even understand how an invention works. Moreover, the Examiner will note that both of the suggested explanations implicate the excision or splicing process. As explained in the accompanying declarations the person of ordinary skill in the art would have known that the process of splicing to excise the intron from the primary transcript is a conserved process, and even though the actual mechanism of enhancement of the gene-silencing may be unknown, the person of ordinary skill in the art would have expected any other intron to function in a similar way during splicing or excision.

The statement of the rejection and the Examiner's alleged reasons for mainatinaing the rejection also imply that the claimed chimreic DNA encompasses an intron anywhere in the chimeric gene and that such constructs are not described. Applicants respectfully submit that, contrary to the implications in the alleged basis for the rejection, the claimed chimeric DNA sequences are not characterized as comprising an intron anywhere in the chimeric gene. Rather, all independent claims indicate that the intron sequence is comprised within the transcribed DNA region.

Applicants maintain that the specification provides adequate written description support for every individual aspect of the claimed invention and the claims taken as a whole as further proven by the evidence submitted herewith. The invention is described in the

specification as claimed in the claims with sufficiently detailed structural elements so that the encompassed genus of chimeric DNA will provide the utilities asserted in the specification for the claimed invention and to distinguish the claimed invention from the teachings of the prior art. The specification provides extensive guidance concerning the general principles of the function of the claimed chimeric gene constructs and provides working examples.

Turning to the evidence newly presented herewith. Each of the declarations of Dr. Elizabeth Salisbury Dennis and Dr. Marc de Block, experts in the field, that are presented herewith pursuant to 37 C.F.R. § 1.132 prove that the teachings of the specification would have demonstrated to a person of ordinary skill in the art that the elements of the invention recited in the claims are sufficient for the claimed chimeric DNA to perform its intended function over the full range encompassed by the claims, i.e. to permit suppression of the expression of any gene of interest using any intronic sequence anywhere in the transcribed region of the dsRNA encoding chimeric gene. These experts have testified that the teachings of the specification would have permitted a person of ordinary skill in the art to make and use a range of chmeric DNA constructs consistent with the scope of the claims from components that were known in the art including a any of a large number of well known intron sequences.

For example, as noted by Dr. Dennis, the Application teaches at least on page 23, lines 5 to 15 that the chimeric DNA constructs of the invention may comprise an intron in the transcribed region that encodes the double-stranded RNA molecule, that the inclusion of the intron enhances the efficiency of reduction of expression of the target nucleic acid interest, and that the intron is preferably (but not necessarily) located in the spacer region. The Application also teaches on page 23, lines 13 to 15 that the intron in a "particularly preferred embodiment" is the *Flaveria trinervia* pyruvate orthophosphate dikinase 2 intron 2 as used in Example 6. DECLARATION OF DR. ELIZABETH SALISBURY DENNIS at ¶ 11.

Thus, Dr. Dennis and Dr. de Block have testified that a person of ordinary skill in the art would have recognized that the description of the recited structural features of the claimed DNA could be combined without limitation with the knowledge of any of the myriad of sequences encompassed by the genus intron and further with the knowledge that insertion of such intron sequence anywhere in the transcribed region of the claimed gene would result in identical dsRNA molecules. DECLARATION OF DR. ELIZABETH SALISBURY DENNIS at ¶ 16.

The Examiner's attention is directed to the accompanying declaration by Dr Elizabeth Salisbury Dennis. Dr Dennis is an expert on the use of introns in genetic constructs. DECLARATION OF DR. ELIZABETH SALISBURY DENNIS at ¶¶ 1-3 and Exhibit 1 attached thereto. Dr. Dennis elaborates on the following points:

- That numerous introns from a wide range of eukaryotic organisms and genes were known and characterized at the date of filing the application. *Id.* at ¶¶ 12, 14
- That introns were known to be removed from primary transcripts by a universally conserved RNA splicing pathway. *Id.* at ¶13.
- That the important structural features for the removal of introns from primary transcripts were known to be highly conserved between different introns. *Id.* at ¶13.
- That a person of ordinary skill in the art would have appreciated the interchangeability of introns in the chimeric constructs of the invention described and claimed in the application. *Id.* at ¶14.
- That it would have been appreciated at the time of the application that intron sequences are removed from the primary transcripts during splicing and that

the resultant spliced dsRNA molecule would be the same irrespective of the exact position of the intron in the transcribed region. *Id.* at ¶15.

Dr. Dennis testified that because of the conserved nature of intron processing, a person of ordinary skill in the art would have immediately appreciated the general interchangeability of the intron that is taught in the specification, i.e. that the intron specifically exemplified in the Application is exchangeable with any other intron sequence. *Id.* at ¶14. Furthermore, Dr. Dennis concluded that a person or ordinary skill in the art would have appreciated and expected that the chimeric genes encoding dsRNA molecules would be functional irrespective of the position of the intron in the transcribed region. *Id.* at ¶15. Accordingly, it is her opinion that when the person of ordinary skill in the art read the teachings of the present application, which include the general usefulness of including an intron in the chimeric DNA, it would have been immediately clear to such person that the teaching of the Application is not limited to the specifically exemplified intron sequence, nor the exemplified preferred location for the intron. *Id.* at ¶16.

Dr Dennis further testified that her opinion is supported by numerous publications, such as those provided by Applicants with the Amendment and Reply filed November 22, 2006 and included as attachments to her declaration, that followed the results first disclosed in the present application. Dr. Dennis noted that several publications reported that by following teachings of the application that were also reported in Smith et al. (2000), persons of ordinary skill in the art were successful in using a variety of intron sequences in the transcribed region of chimeric DNA such as presently claimed. *Id.* at ¶17 and Exhibits 3-12 attached thereto.

The Examiner's attention is also drawn to the declaration of Dr Marc De Block, stating that his opinion, based upon personal experience, that a person skilled in the art would

have immediately understood that the applicability of the inventions described in the Application is not limited to the specific Example therein, nor to the particular intron used in that Example. DECLARATION OF DR. MARC DE BLOCK at ¶17. Dr. De Block testifies that a person of ordinary skill in the art would have understood that the exemplified intron could be exchanged for other well known introns (which would function in the same manner, since the process of removal of introns from RNA molecules is a conserved process). *Id.* at ¶14. His opinion is supported by his personal experience upon learning of the results disclosed in the present application and applying that learning to his own project in the context of a licensing of the invention described in the application and subsequent collaboration with applicants. Id. ¶ 10-12. Indeed, upon being informed of the increased efficiency in gene-silencing obtained by the inclusion of an intron in the transcribed region of the dsRNA encoding chimeric gene Dr De Block immediately included an intron in the design of the gene silencing constructs for the particular project he was working on. *Id.* at 12. However, Dr De Block did not include the exemplified pyruvate orthophosphate dikinase 2 intron from *Flaveria trinervia*, but instead used another well known intron sequence with similar effect. *Id.* at ¶¶13-14.

The declarations provided herewith prove unequivocally that the teachings of the present application satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. As explained in *Capon v. Eshhar*, "[t]he 'written description' requirement implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed." *Capon v. Eshhar*, 418 F.3d 1349, 1357,

76 U.S.P.Q.2d 1078 (Fed. Cir. 2005). Both Dr. Dennis and Dr. De Block have testified and provided reasons as to why the present application satisfies the requirement.

Applicants respectfully submit that each declaration presented herewith effectively refutes the allegation by the Office that the specification does not adequately describe chimeric DNA comprising any intron inserted anywhere in the transcribed region of the claimed chimeric DNA that would perform the functions asserted in the specification. In view of the general applicability of the invention, the Office cannot reasonably expect and it is well established that it is not required that Applicants provide a working example, or even list, every known intron sequence. *Falkner v. Inglis*, 79 U.S.P.Q.2d 1001, 1008 (Fed. Cir. 2006)("it is binding precedent of this court that Eli Lilly does not set forth a per se rule that whenever a claim limitation is directed to a macromolecular sequence, the specification must always recite the gene or sequence, regardless of whether it is known in the prior art"); see also *Monsanto Co. v. Scruggs*, 79 USPQ2d 1813, 1818 (Fed. Cir. 2006)("At the time of the 605 patent application, those of ordinary skill in the art knew the DNA sequences of several strains of the CaMV virus, the location of the CaMV promoters and the DNA sequences for several CaMV35S promoters. Given the knowledge in the art, it was unnecessary for the '605 patent to include specific gene sequences when referring to the CaMV 35S promoter to meet the written description requirement.").

There was no need in the present application to describe more specific intron sequences than those presented in the working examples, because at the time of filing the current application, other intron sequences were well known. The working examples of an application need not explicitly span the full scope the claim language to support the adequacy of a written description. *Falkner,* 79 U.S.P.Q.2d at 1007 ("A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain

examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation.")(citing *Lizard Tech, Inc v. Earth Resource Mapping PTY, Inc*, 424 F.3d 1336, 1345, 76 USPQ2d 1724 (Fed. Cir. 2005); *see also Union Oil Co. v. Atantic. Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227 (Fed. Cir. 2000); *In re GPAC Inc.*, 57 F.3d 1573, 1579, 35 USPQ2d 1116 (Fed. Cir. 1995)).

Applicants have responded to the specific remarks in the Office Action mailed February 8, 2007 regarding Applicants arguments and have shown that that Office did not fully appreciate the nature of what Applicants evidence had previously shown. Applicants have also provided further evidence in two affidavits pursuant to 37 C.F.R. § 1.132 proving that a person of ordinary skill reading the application at the time that it was filed would have immediately appreciated that the inventors were in possession of the invention presently claimed in each particular aspect and as a whole. For all the reasons that have been presented, withdrawal of the rejection is appropriate and is respectfully requested.

Request for rejoinder of process claims 1-10, 12, 40, 43, 44, 46, 50, 70-84, 98, 99, 104, and 105.

The withdrawn process claims 1-10, 12, 40, 43, 44, 46, 50, 70-84, 98, 99, 104, and 105 include all the limitations of the product claims under consideration. Accordingly, Applicant requests that the restriction between withdrawn process claims 1-10, 12, 40, 43, 44,

46, 50, 70-84, 98, 99, 104, and 105 and product claims 22, 26, 42, 53, 54, 56, 58, 63-69, 85-97, 100-103 and 106-108 be withdrawn in accordance with Manual of Patent Examination Procedure § 806.05(h). The process claims should be considered for rejoinder, and fully examined for patentability.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

The Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

Date: August 8, 2007

By: _____
Christopher L. North
Registration No. 50433

P.O. Box 1404
Alexandria, VA 22313-1404
703 836 6620